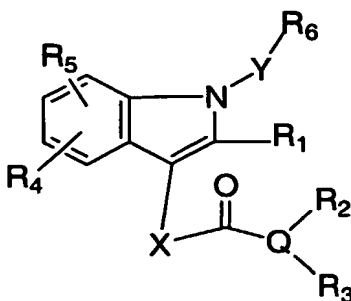


WHAT IS CLAIMED IS:

1. A compound of the structural formula I:



Formula I

or a pharmaceutically acceptable salt, enantiomer, diastereomer or mixture thereof:

wherein,

R represents hydrogen, or C<sub>1-6</sub> alkyl;

R<sub>1</sub> represents hydrogen or C<sub>1-6</sub> alkyl, CF<sub>3</sub>, C<sub>1-6</sub> alkoxy, OH, COR<sup>c</sup>, CO<sub>2</sub>R<sub>8</sub>,

CONHCH<sub>2</sub>CO<sub>2</sub>R, N(R)<sub>2</sub>, said alkyl and alkoxy optionally substituted with 1-3 groups selected from R<sup>b</sup>;

X represents -(CHR<sub>7</sub>)<sub>p</sub>;

Y represents -CO(CH<sub>2</sub>)<sub>n</sub>-, or -CH(OR)-;

Q represents N, CR<sub>Y</sub>, or O, wherein R<sub>2</sub> is absent when Q is O;

R<sub>Y</sub> represents H, or C<sub>1-6</sub> alkyl;

R<sub>w</sub> represents H, C<sub>1-6</sub> alkyl, -C(O)C<sub>1-6</sub> alkyl, -C(O)OC<sub>1-6</sub> alkyl, -SO<sub>2</sub>N(R)<sub>2</sub>, -SO<sub>2</sub>C<sub>1-6</sub> alkyl, -SO<sub>2</sub>C<sub>6-10</sub> aryl, NO<sub>2</sub>, CN or -C(O)N(R)<sub>2</sub>;

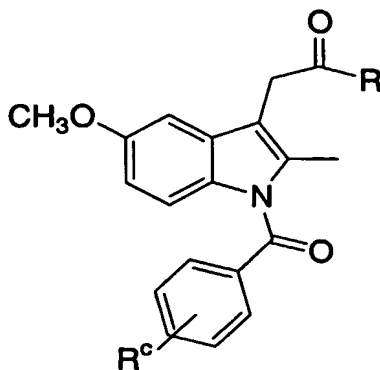
- R<sub>2</sub> represents hydrogen, C<sub>1-10</sub> alkyl, C<sub>1-6</sub> alkylSR, -(CH<sub>2</sub>)<sub>n</sub>O(CH<sub>2</sub>)<sub>m</sub>OR, -(CH<sub>2</sub>)<sub>n</sub>C<sub>1-6</sub> alkoxy, -(CH<sub>2</sub>)<sub>n</sub>C<sub>3-8</sub> cycloalkyl, -(CH<sub>2</sub>)<sub>n</sub>C<sub>3-10</sub> heterocyclyl, -(CH<sub>2</sub>)<sub>n</sub>C<sub>5-10</sub> heteroaryl, -N(R)<sub>2</sub>, -COOR, or -(CH<sub>2</sub>)<sub>n</sub>C<sub>6-10</sub> aryl, said alkyl, heterocyclyl, aryl or heteroaryl  
 5 optionally substituted with 1-3 groups selected from R<sup>a</sup>;
- R<sub>3</sub> represents hydrogen, C<sub>1-10</sub> alkyl, -(CH<sub>2</sub>)<sub>n</sub>C<sub>3-8</sub> cycloalkyl, -(CH<sub>2</sub>)<sub>n</sub>C<sub>3-10</sub> heterocyclyl, -(CH<sub>2</sub>)<sub>n</sub>C<sub>5-10</sub> heteroaryl, -(CH<sub>2</sub>)<sub>n</sub>COOR, -(CH<sub>2</sub>)<sub>n</sub>C<sub>6-10</sub> aryl, -(CH<sub>2</sub>)<sub>n</sub>NHR<sub>8</sub>, -(CH<sub>2</sub>)<sub>n</sub>N(R)<sub>2</sub>, -(CH<sub>2</sub>)<sub>n</sub>N(R<sub>8</sub>)<sub>2</sub>, -(CH<sub>2</sub>)<sub>n</sub>NHCOOR, -(CH<sub>2</sub>)<sub>n</sub>N(R<sub>8</sub>)CO<sub>2</sub>R, -(CH<sub>2</sub>)<sub>n</sub>N(R<sub>8</sub>)COR, -  
 10 (CH<sub>2</sub>)<sub>n</sub>NHCOR, -(CH<sub>2</sub>)<sub>n</sub>CONH(R<sub>8</sub>), aryl, -(CH<sub>2</sub>)<sub>n</sub>C<sub>1-6</sub>-OR, CF<sub>3</sub>, -(CH<sub>2</sub>)<sub>n</sub>SO<sub>2</sub>R, -(CH<sub>2</sub>)<sub>n</sub>SO<sub>2</sub>N(R)<sub>2</sub>, -(CH<sub>2</sub>)<sub>n</sub>CON(R)<sub>2</sub>, -(CH<sub>2</sub>)<sub>n</sub>CONHC(R)<sub>3</sub>, -(CH<sub>2</sub>)<sub>n</sub>CONHC(R)<sub>2</sub>CO<sub>2</sub>R, -(CH<sub>2</sub>)<sub>n</sub>COR<sub>8</sub>, nitro, cyano or halogen, said alkyl, alkoxy, heterocyclyl, aryl or heteroaryl  
 optionally substituted with 1-3 groups of R<sup>a</sup>;
- 15 or, when Q is N, R<sub>2</sub> and R<sub>3</sub> taken together with the intervening N atom form a 4-10 membered heterocyclic carbon ring optionally interrupted by 1-2 atoms of O, S, C(O) or NR, and optionally having 1-4 double bonds, and optionally substituted by 1-3 groups selected from R<sup>a</sup>;
- R<sub>4</sub> and R<sub>5</sub> independently represent hydrogen, C<sub>1-6</sub> alkoxy, OH, C<sub>1-6</sub> alkyl, COOR, SO<sub>3</sub>H, C<sub>1-6</sub> alkylcarbonyl, S(O)qRY, -O(CH<sub>2</sub>)<sub>n</sub>N(R)<sub>2</sub>, -O(CH<sub>2</sub>)<sub>n</sub>CO<sub>2</sub>R, -OPO(OH)<sub>2</sub>, CF<sub>3</sub>, -N(R)<sub>2</sub>, nitro, cyano, C<sub>1-6</sub> alkylamino, or halogen;  
 20
- R<sub>6</sub> represents hydrogen, C<sub>1-10</sub> alkyl, -(CH<sub>2</sub>)<sub>n</sub>C<sub>6-10</sub> aryl, -NH(CH<sub>2</sub>)<sub>n</sub>C<sub>6-10</sub> aryl, -(CH<sub>2</sub>)<sub>n</sub>C<sub>5-10</sub> heteroaryl, -NH(CH<sub>2</sub>)<sub>n</sub>C<sub>5-10</sub> heteroaryl, (C<sub>6-10</sub> aryl)O-, -(CH<sub>2</sub>)<sub>n</sub>C<sub>3-10</sub> heterocyclyl, -(CH<sub>2</sub>)<sub>n</sub>C<sub>3-8</sub> cycloalkyl, -COOR, -C(O)CO<sub>2</sub>R, said aryl, heteroaryl, heterocyclyl  
 25 and alkyl optionally substituted with 1-3 groups selected from R<sup>a</sup>;
- R<sub>7</sub> represents hydrogen, C<sub>1-6</sub> alkyl, -(CH<sub>2</sub>)<sub>n</sub>COOR or -(CH<sub>2</sub>)<sub>n</sub>N(R)<sub>2</sub>,
- 30 R<sub>8</sub> represents -(CH<sub>2</sub>)<sub>n</sub>C<sub>3-8</sub> cycloalkyl, -(CH<sub>2</sub>)<sub>n</sub> 3-10 heterocyclyl, C<sub>1-6</sub> alkoxy or -(CH<sub>2</sub>)<sub>n</sub>C<sub>5-10</sub> heteroaryl, -(CH<sub>2</sub>)<sub>n</sub>C<sub>6-10</sub> aryl said heterocyclyl, aryl or heteroaryl optionally substituted with 1-3 groups selected from R<sup>a</sup>;

- $R^a$  represents F, Cl, Br, I,  $CF_3$ ,  $N(R)_2$ ,  $NO_2$ , CN,  $-(CH_2)_nCOR_8$ ,  $-(CH_2)_nCONHR_8$ ,  $-(CH_2)_nCON(R_8)_2$ ,  $-O(CH_2)_nCOOR$ ,  $-NH(CH_2)_nOR$ ,  $-COOR$ ,  $-OCF_3$ ,  $-NHCOR$ ,  $-SO_2R$ ,  $-SO_2NR_2$ ,  $-SR$ ,  $(C_1-C_6 \text{ alkyl})O-$ ,  $-(CH_2)_nO(CH_2)_mOR$ ,  $-(CH_2)_nC_{1-6} \text{ alkoxy}$ ,  $(\text{aryl})O-$ ,  $-OH$ ,  $(C_1-C_6 \text{ alkyl})S(O)_m-$ ,  $H_2N-C(NH)-$ ,  $(C_1-C_6 \text{ alkyl})C(O)-$ ,  $(C_1-C_6 \text{ alkyl})OC(O)NH-$ ,  $-(C_1-C_6 \text{ alkyl})NR_w(CH_2)_nC_{3-10} \text{ heterocyclyl-}R_w$ ,  $-(C_1-C_6 \text{ alkyl})O(CH_2)_nC_{3-10} \text{ heterocyclyl-}R_w$ ,  $-(C_1-C_6 \text{ alkyl})S(CH_2)_nC_{3-10} \text{ heterocyclyl-}R_w$ ,  $-(C_1-C_6 \text{ alkyl})-C_{3-10} \text{ heterocyclyl-}R_w$ ,  $-(CH_2)_n-Z^1-C(=Z^2)N(R)_2$ ,  $-(C_{2-6} \text{ alkenyl})NR_w(CH_2)_nC_{3-10} \text{ heterocyclyl-}R_w$ ,  $-(C_{2-6} \text{ alkenyl})O(CH_2)_nC_{3-10} \text{ heterocyclyl-}R_w$ ,  $-(C_{2-6} \text{ alkenyl})S(CH_2)_nC_{3-10} \text{ heterocyclyl-}R_w$ ,  $-(C_{2-6} \text{ alkenyl})-C_{3-10} \text{ heterocyclyl-}R_w$ ,  $-(C_{2-6} \text{ alkenyl})-Z^1-C(=Z^2)N(R)_2$ ,  $-(CH_2)_nSO_2R$ ,  $-(CH_2)_nSO_3H$ ,  $-(CH_2)_nPO(OR)_2$ , cyclohexyl, morpholinyl, piperidyl, pyrrolidinyl, thiophenyl, phenyl, pyridyl, imidazolyl, oxazolyl, isoxazolyl, thiazolyl, thienyl, furyl, isothiazolyl,  $C_{2-6} \text{ alkenyl}$ , and  $C_1-C_{10} \text{ alkyl}$ , said alkyl, alkenyl, alkoxy, phenyl, pyridyl, imidazolyl, oxazolyl, isoxazolyl, thiazolyl, thienyl, furyl, and isothiazolyl optionally substituted with 1-3 groups selected from  $C_1-C_6 \text{ alkyl}$ , and  $COOR$ ;
- $Z^1$  and  $Z^2$  independently represents  $NR_w$ , O,  $CH_2$ , or S;
- $R^b$  represents  $C_{1-6} \text{ alkyl}$ ,  $-COOR$ ,  $-SO_3R$ ,  $-OPO(OH)_2$ ,  $-(CH_2)_nC_{6-10} \text{ aryl}$ , or  $-(CH_2)_nC_{5-10} \text{ heteroaryl}$ ;
- $R^c$  represents hydrogen,  $C_{1-6} \text{ alkyl}$ , or  $-(CH_2)_nC_{6-10} \text{ aryl}$ ;
- $m$  is 0-3;  
 $n$  is 0-3;  
 $q$  is 0-2; and  
 $p$  is 0-1.

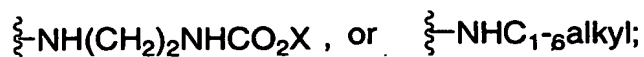
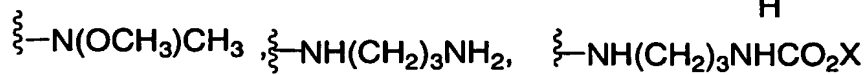
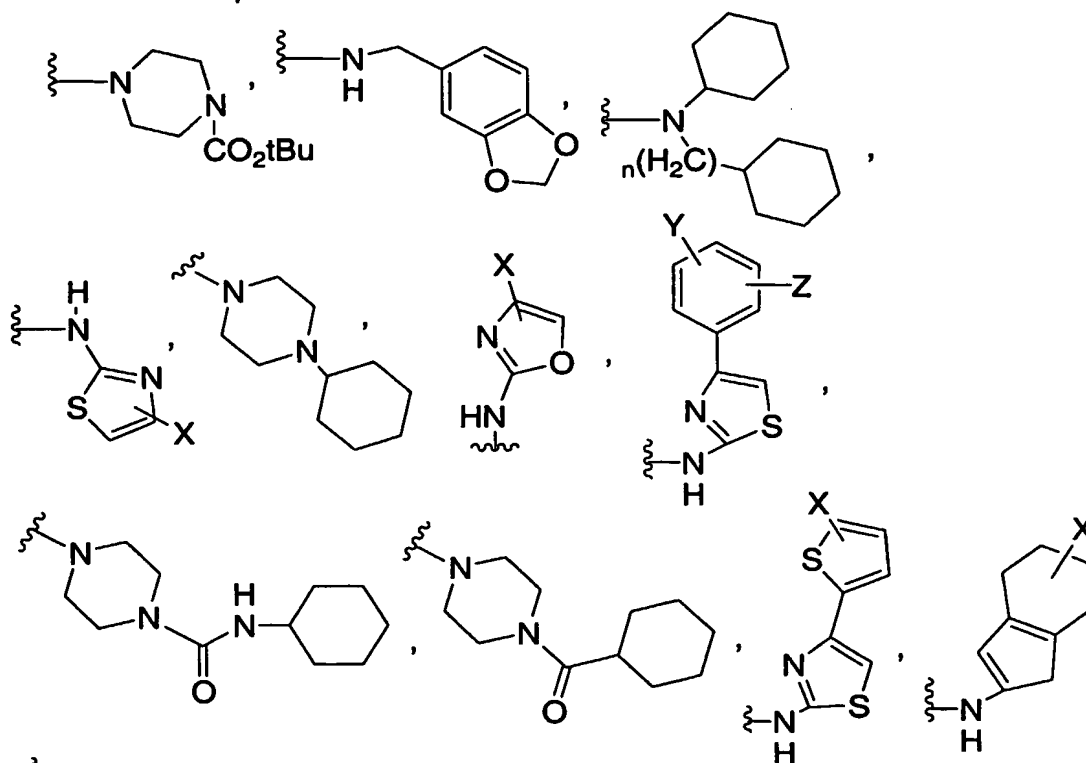
2. A compound of the structural formula I wherein X is  $CHR_7$ .
3. A compound according to claim 1 wherein Y is  $-CO(CH_2)_n$ .
4. A compound according to claim 1 wherein Y is  $CH(OR)$ .

- 5
5. A compound according to claim 1 wherein Q is N.
6. A compound according to claim 1 wherein Q is CH.
7. A compound according to claim 2 wherein R<sub>6</sub> is (CH<sub>2</sub>)<sub>n</sub>C<sub>6-10</sub> aryl, (CH<sub>2</sub>)<sub>n</sub>C<sub>5-10</sub> heteroaryl, (CH<sub>2</sub>)<sub>n</sub>C<sub>3-10</sub> heterocyclyl, or (CH<sub>2</sub>)<sub>n</sub>C<sub>3-8</sub> cycloalkyl, said aryl, heteroaryl, heterocyclyl and alkyl optionally substituted with 1 to 3 groups of R<sup>a</sup>.
- 10
8. A compound according to claim 6 wherein R<sub>7</sub> is hydrogen or C<sub>1-6</sub> alkyl.
9. A compound according to claim 6 wherein Q is N and n is 0.
10. A compound according to claim 1 wherein Y is -CO(CH<sub>2</sub>)<sub>n</sub>, Q is N, n is 0, R<sub>2</sub> is C<sub>1-10</sub> alkyl or C<sub>1-6</sub> alkylOH and R<sub>3</sub> is (CH<sub>2</sub>)<sub>n</sub>C<sub>3-10</sub> heterocyclyl, said heterocyclyl and alkyl optionally substituted with 1 to 3 groups of R<sup>a</sup>.
- 15
11. A compound which is selected from Tables 1 through 4:

Table 1

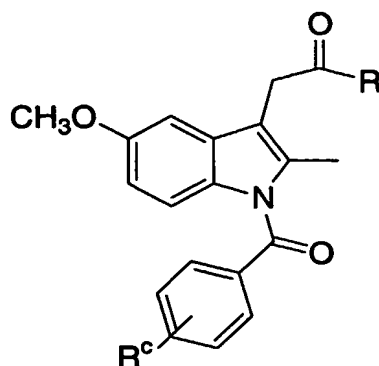


Wherein R represents:

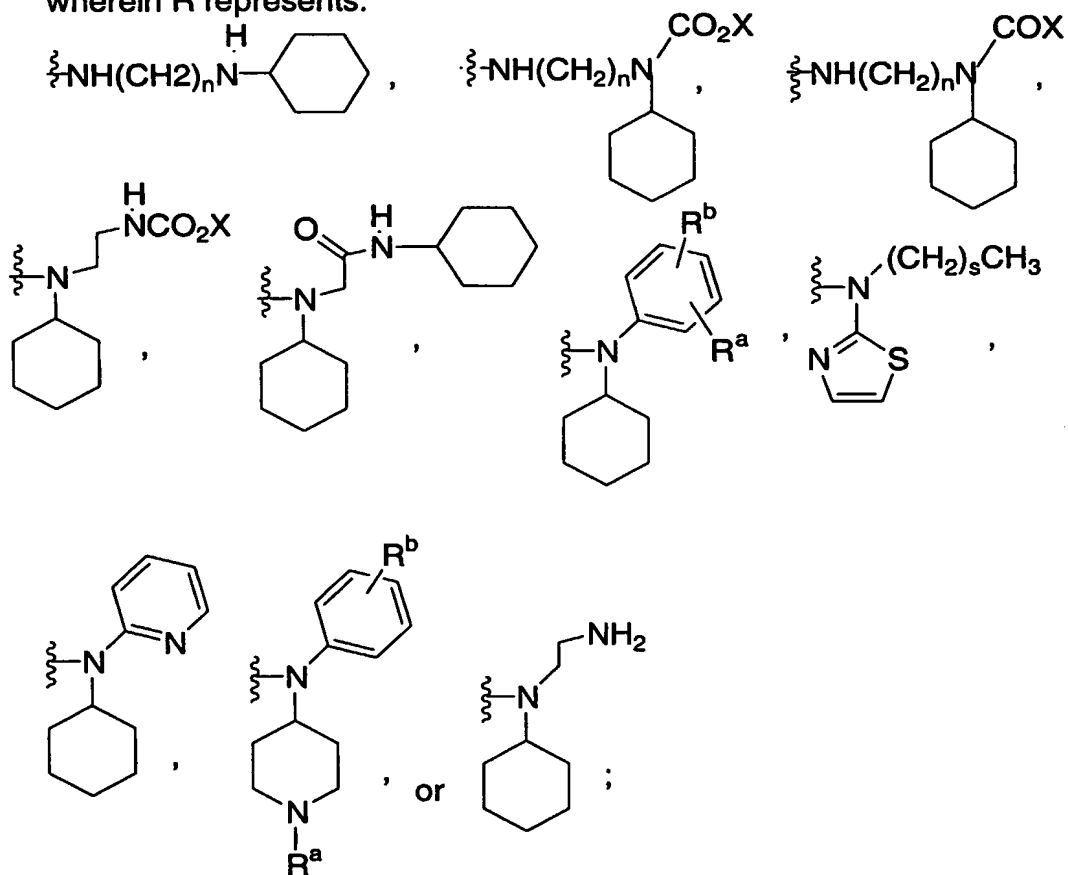


n is 0 to 3; X, Y and Z, independently represent hydrogen or  $C_{1-6}$  alkyl; and  $R_c$  represents hydrogen, halogen,  $C_{1-6}$  alkyl,  $CF_3$ ,  $OCF_3$ ,  $N(CH_3)_3$ ,  $COC_{1-6}$  alkyl, or methoxy;

Table 2

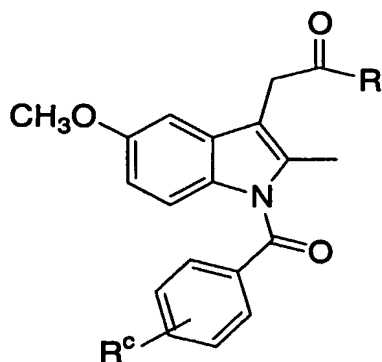


wherein R represents:

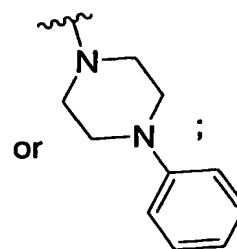
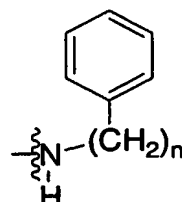
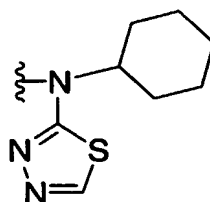
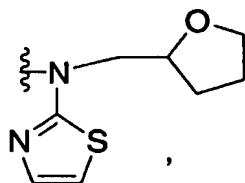
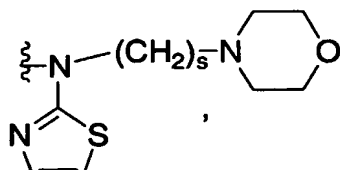
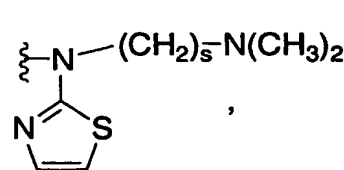
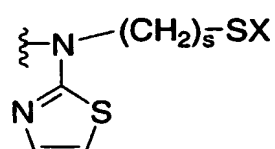
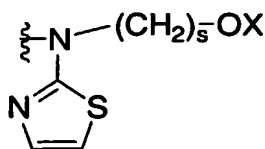
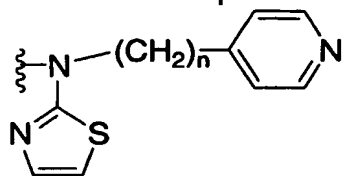


n is 0 to 3; s is 1-5; X represents hydrogen or C<sub>1-6</sub> alkyl; R<sup>b</sup> and R<sup>a</sup> independently represent hydrogen, methoxy, CO<sub>2</sub>X, NHAc, or C<sub>1-6</sub> alkyl; R<sup>c</sup> represents hydrogen, halogen, C<sub>1-6</sub> alkyl, CF<sub>3</sub>, OCF<sub>3</sub>, N(CH<sub>3</sub>)<sub>2</sub>, COC<sub>1-6</sub> alkyl, or methoxy

Table 3

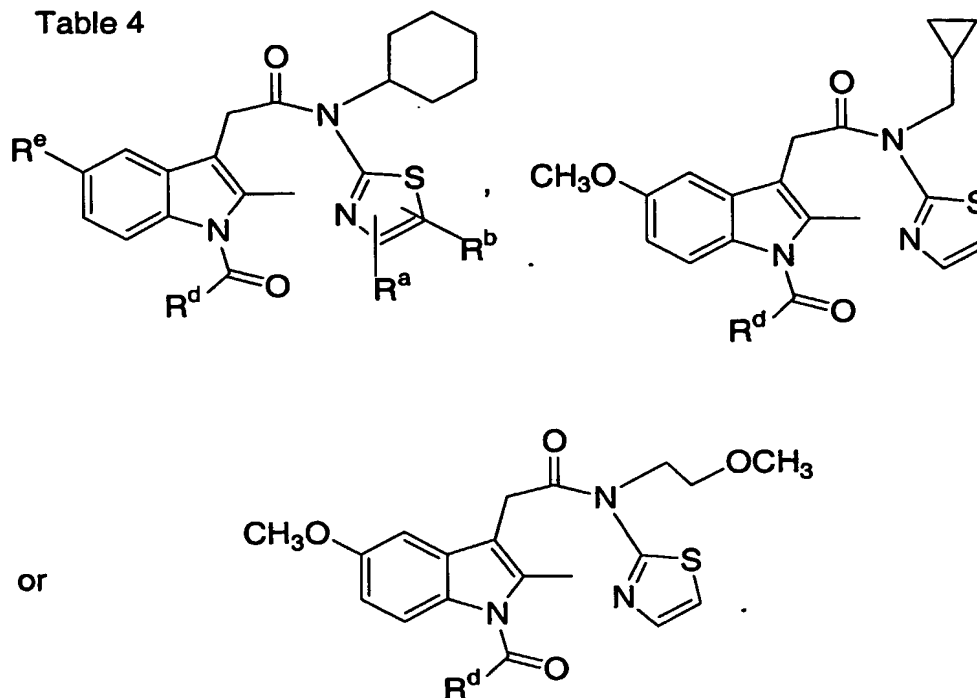


wherein R represents:



n is 0 to 3; s is 1-5; X represents hydrogen or C<sub>1-6</sub> alkyl; and R<sup>c</sup> represents hydrogen, halogen, C<sub>1-6</sub> alkyl, CF<sub>3</sub>, OCF<sub>3</sub>, N(CH<sub>3</sub>)<sub>2</sub>, COC<sub>1-6</sub> alkyl, or methoxy

Table 4



wherein:

$R^b$  and  $R^a$  independently represent hydrogen, methoxy,  $CO_2X$ ,  $NHAc$ , or  $C_{1-6}$  alkyl;

$R^d$  represents  $C_{1-6}$  alkyl, pyridinyl, -O-phenyl, phenyl, thienyl, said pyridinyl and phenyl optionally substituted with 1-3 halogen,  $CF_3$ ,  $OCF_3$ ,  $N(CH_3)_2$ , methoxy or  $C_{1-6}$  alkyl; and

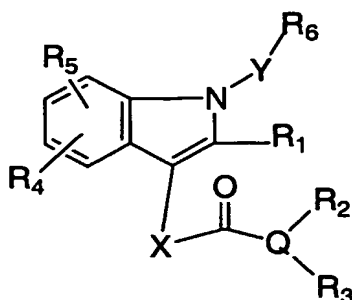
$R^e$  represents methoxy,  $O(CH_2)_2N(CH_3)_2$ , or  $OH$ ;

or a pharmaceutically acceptable salt, enantiomer, diastereomer or mixture thereof.

- 5                    12.    A method for treating ocular hypertension or glaucoma comprising administration to a patient in need of such treatment a therapeutically effective amount of a



compound of structural formula I:



5

Formula I

or a pharmaceutically acceptable salt, enantiomer, diastereomer or mixture thereof:  
wherein,

10 R represents hydrogen, or C<sub>1-6</sub> alkyl;

R<sub>1</sub> represents hydrogen or C<sub>1-6</sub> alkyl, CF<sub>3</sub>, C<sub>1-6</sub> alkoxy, OH, COR<sup>c</sup>, CO<sub>2</sub>R<sub>8</sub>,  
CONHCH<sub>2</sub>CO<sub>2</sub>R, N(R)<sub>2</sub>, said alkyl and alkoxy optionally substituted with 1-3 groups selected  
from R<sup>b</sup>;

15

X represents -(CHR<sup>7</sup>)<sub>p</sub>-;

Y represents -CO(CH<sub>2</sub>)<sub>n</sub>-, or -CH(OR)-;

20 Q represents N, CR<sup>y</sup>, or O, wherein R<sub>2</sub> is absent when Q is O;

R<sup>y</sup> represents H, or C<sub>1-6</sub> alkyl;

R<sub>w</sub> represents H, C<sub>1-6</sub> alkyl, -C(O)C<sub>1-6</sub> alkyl, -C(O)OC<sub>1-6</sub> alkyl, -SO<sub>2</sub>N(R)<sub>2</sub>, -SO<sub>2</sub>C<sub>1-6</sub> alkyl,  
25 -SO<sub>2</sub>C<sub>6-10</sub> aryl, NO<sub>2</sub>, CN or -C(O)N(R)<sub>2</sub>;

R<sub>2</sub> represents hydrogen, C<sub>1-10</sub> alkyl, C<sub>1-6</sub> alkylSR, -(CH<sub>2</sub>)<sub>n</sub>O(CH<sub>2</sub>)<sub>m</sub>OR,

$-(CH_2)_n C_{1-6}$  alkoxy,  $-(CH_2)_n C_{3-8}$  cycloalkyl,  $-(CH_2)_n C_{3-10}$  heterocyclyl,  $-(CH_2)_n C_{5-10}$  heteroaryl,  $-N(R)_2$ ,  $-COOR$ , or  $-(CH_2)_n C_{6-10}$  aryl, said alkyl, heterocyclyl, aryl or heteroaryl optionally substituted with 1-3 groups selected from  $R^a$ ;

- 5  $R_3$  represents hydrogen,  $C_{1-10}$  alkyl,  $-(CH_2)_n C_{3-8}$  cycloalkyl,  $-(CH_2)_n C_{3-10}$  heterocyclyl,  $-(CH_2)_n C_{5-10}$  heteroaryl,  $-(CH_2)_n COOR$ ,  $-(CH_2)_n C_{6-10}$  aryl,  $-(CH_2)_n NHR_8$ ,  $-(CH_2)_n N(R)_2$ ,  $-(CH_2)_n N(R_8)_2$ ,  $-(CH_2)_n NHCOOR$ ,  $-(CH_2)_n N(R_8)CO_2R$ ,  $-(CH_2)_n N(R_8)COR$ ,  $-(CH_2)_n NHCOR$ ,  $-(CH_2)_n CONH(R_8)$ , aryl,  $-(CH_2)_n C_{1-6}-OR$ ,  $CF_3$ ,  $-(CH_2)_n SO_2R$ ,  $-(CH_2)_n SO_2N(R)_2$ ,  $-(CH_2)_n CON(R)_2$ ,  $-(CH_2)_n CONHC(R)_3$ ,  $-(CH_2)_n CONHC(R)_2CO_2R$ ,  $-(CH_2)_n COR_8$ , nitro, cyano or halogen, said alkyl, alkoxy, heterocyclyl, aryl or heteroaryl  
10 optionally substituted with 1-3 groups of  $R^a$ ;

- or, when  $Q$  is  $N$ ,  $R_2$  and  $R_3$  taken together with the intervening  $N$  atom form a 4-10 membered heterocyclic carbon ring optionally interrupted by 1-2 atoms of  $O$ ,  $S$ ,  $C(O)$  or  $NR$ , and optionally  
15 having 1-4 double bonds, and optionally substituted by 1-3 groups selected from  $R^a$ ;

$R_4$  and  $R_5$  independently represent hydrogen,  $C_{1-6}$  alkoxy,  $OH$ ,  $C_{1-6}$  alkyl,  $COOR$ ,  $SO_3H$ ,  $C_{1-6}$  alkylcarbonyl,  $S(O)_qRY$ ,  $-O(CH_2)_n N(R)_2$ ,  $-O(CH_2)_n CO_2R$ ,  $-OPO(OH)_2$ ,  $CF_3$ ,  $-N(R)_2$ , nitro, cyano,  $C_{1-6}$  alkylamino, or halogen;

- 20  $R_6$  represents hydrogen,  $C_{1-10}$  alkyl,  $-(CH_2)_n C_{6-10}$  aryl,  $-NH(CH_2)_n C_{6-10}$  aryl,  $-(CH_2)_n C_{5-10}$  heteroaryl,  $-NH(CH_2)_n C_{5-10}$  heteroaryl,  $(C_{6-10} \text{ aryl})O-$ ,  $-(CH_2)_n C_{3-10}$  heterocyclyl,  $-(CH_2)_n C_{3-8}$  cycloalkyl,  $-COOR$ ,  $-C(O)CO_2R$ , said aryl, heteroaryl, heterocyclyl and alkyl optionally substituted with 1-3 groups selected from  $R^a$ ;

- 25  $R_7$  represents hydrogen,  $C_{1-6}$  alkyl,  $-(CH_2)_n COOR$  or  $-(CH_2)_n N(R)_2$ ,

- $R_8$  represents  $-(CH_2)_n C_{3-8}$  cycloalkyl,  $-(CH_2)_n C_{3-10}$  heterocyclyl,  $C_{1-6}$  alkoxy or  $-(CH_2)_n C_{5-10}$  heteroaryl,  $-(CH_2)_n C_{6-10}$  aryl said heterocyclyl, aryl or heteroaryl optionally substituted with  
30 1-3 groups selected from  $R^a$ ;

$R^a$  represents  $F$ ,  $Cl$ ,  $Br$ ,  $I$ ,  $CF_3$ ,  $N(R)_2$ ,  $NO_2$ ,  $CN$ ,  $-(CH_2)_n COR_8$ ,  $-(CH_2)_n CONHR_8$ ,  $-(CH_2)_n CON(R_8)_2$ ,  $-O(CH_2)_n COOR$ ,  $-NH(CH_2)_n OR$ ,  $-COOR$ ,  $-OCF_3$ ,  $-NHCOR$ ,  $-SO_2R$ ,  $-SO_2NR_2$ ,  $-SR$ ,  $(C_1-C_6 \text{ alkyl})O-$ ,  $-(CH_2)_n O(CH_2)_m OR$ ,  $-(CH_2)_n C_{1-6}$  alkoxy,  $(\text{aryl})O-$ ,  $-OH$ ,

(C<sub>1</sub>-C<sub>6</sub> alkyl)S(O)<sub>m</sub>-, H<sub>2</sub>N-C(NH)-, (C<sub>1</sub>-C<sub>6</sub> alkyl)C(O)-, (C<sub>1</sub>-C<sub>6</sub> alkyl)OC(O)NH-, -(C<sub>1</sub>-C<sub>6</sub> alkyl)NR<sub>w</sub>(CH<sub>2</sub>)<sub>n</sub>C<sub>3-10</sub> heterocyclyl-R<sub>w</sub>, -(C<sub>1</sub>-C<sub>6</sub> alkyl)O(CH<sub>2</sub>)<sub>n</sub>C<sub>3-10</sub> heterocyclyl-R<sub>w</sub>, -(C<sub>1</sub>-C<sub>6</sub> alkyl)S(CH<sub>2</sub>)<sub>n</sub>C<sub>3-10</sub> heterocyclyl-R<sub>w</sub>, -(C<sub>1</sub>-C<sub>6</sub> alkyl)-C<sub>3-10</sub> heterocyclyl-R<sub>w</sub>, -(CH<sub>2</sub>)<sub>n</sub>-Z<sup>1</sup>-C(=Z<sup>2</sup>)N(R)<sub>2</sub>, -(C<sub>2-6</sub> alkenyl)NR<sub>w</sub>(CH<sub>2</sub>)<sub>n</sub>C<sub>3-10</sub> heterocyclyl-R<sub>w</sub>, -(C<sub>2-6</sub> alkenyl)O(CH<sub>2</sub>)<sub>n</sub>C<sub>3-10</sub> heterocyclyl-R<sub>w</sub>, -(C<sub>2-6</sub> alkenyl)S(CH<sub>2</sub>)<sub>n</sub>C<sub>3-10</sub> heterocyclyl-R<sub>w</sub>, -(C<sub>2-6</sub> alkenyl)-C<sub>3-10</sub> heterocyclyl-R<sub>w</sub>, -(C<sub>2-6</sub> alkenyl)-Z<sup>1</sup>-C(=Z<sup>2</sup>)N(R)<sub>2</sub>, -(CH<sub>2</sub>)<sub>n</sub>SO<sub>2</sub>R, -(CH<sub>2</sub>)<sub>n</sub>SO<sub>3</sub>H, -(CH<sub>2</sub>)<sub>n</sub>PO(OR)<sub>2</sub>, cyclohexyl, morpholinyl, piperidyl, pyrrolidinyl, thiophenyl, phenyl, pyridyl, imidazolyl, oxazolyl, isoxazolyl, thiazolyl, thienyl, furyl, isothiazolyl, C<sub>2-6</sub> alkenyl, and C<sub>1</sub>-C<sub>10</sub> alkyl, said alkyl, alkenyl, alkoxy, phenyl, pyridyl, imidazolyl, oxazolyl, isoxazolyl, thiazolyl, thienyl, furyl, and isothiazolyl optionally substituted with 1-3 groups selected from C<sub>1</sub>-C<sub>6</sub> alkyl, and COOR;

Z<sup>1</sup> and Z<sup>2</sup> independently represents NR<sub>w</sub>, O, CH<sub>2</sub>, or S;

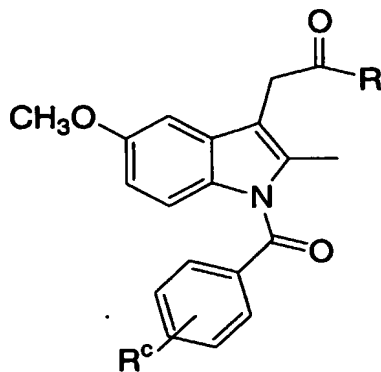
R<sup>b</sup> represents C<sub>1-6</sub> alkyl, -COOR, -SO<sub>3</sub>R, -OPO(OH)<sub>2</sub>, -(CH<sub>2</sub>)<sub>n</sub>C<sub>6-10</sub> aryl, or -(CH<sub>2</sub>)<sub>n</sub>C<sub>5-10</sub> heteroaryl;

R<sup>c</sup> represents hydrogen, C<sub>1-6</sub> alkyl, or -(CH<sub>2</sub>)<sub>n</sub>C<sub>6-10</sub> aryl;

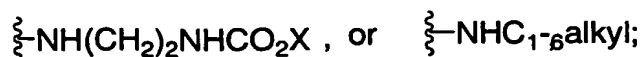
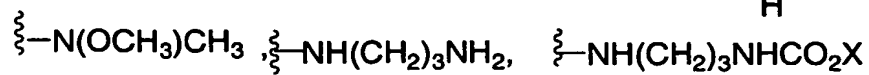
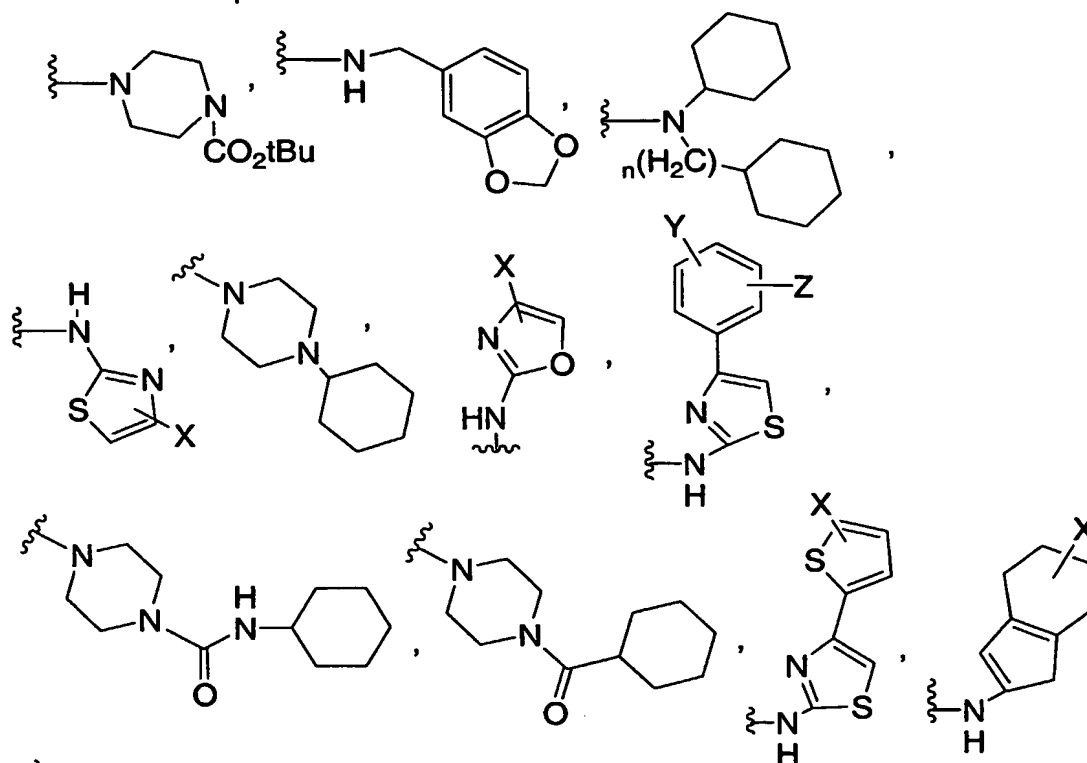
m is 0-3;  
 n is 0-3;  
 q is 0-2; and  
 p is 0-1.

13. The method according to claim 12 wherein the compound of Formula I is selected from Tables 1 through 4:

### Table 1

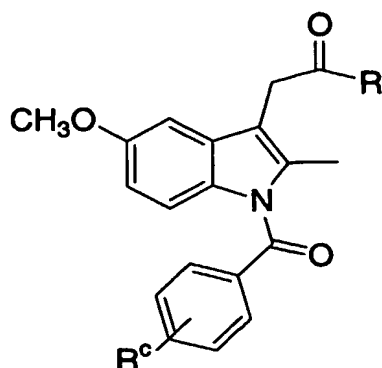


**Wherein R represents:**

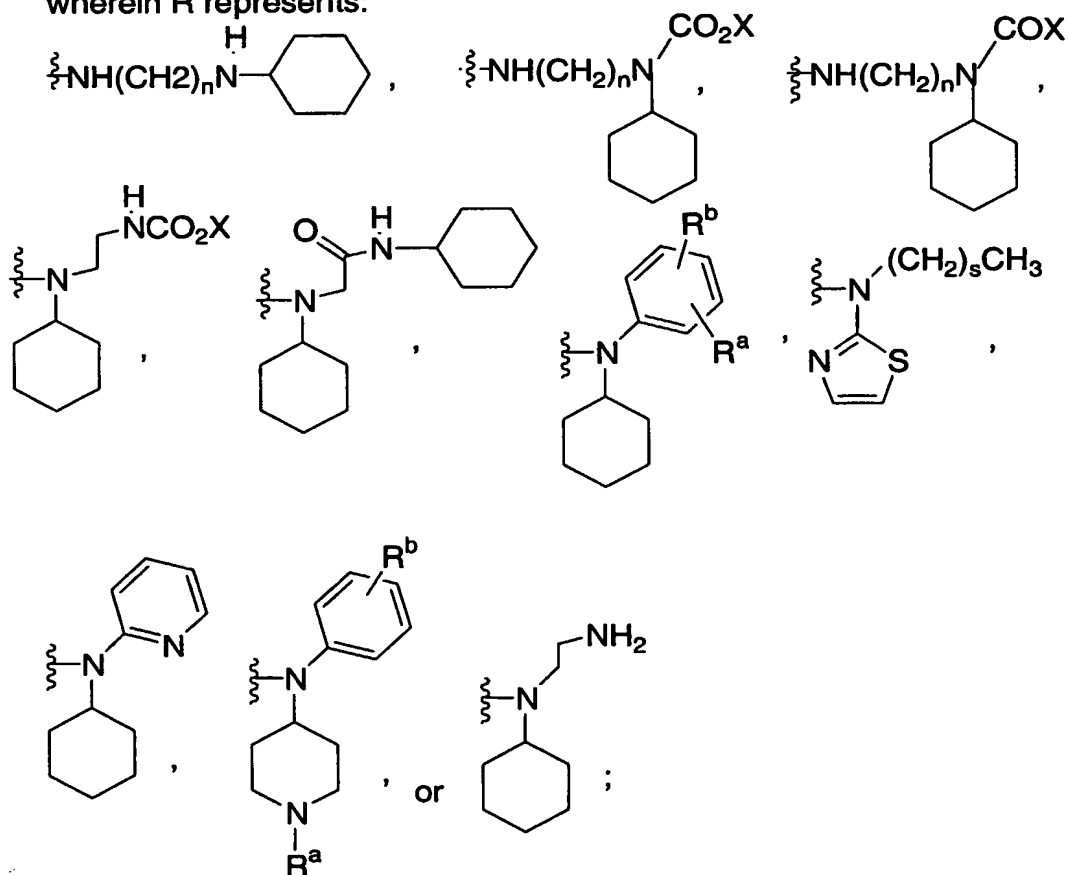


n is 0 to 3; X, Y and Z, independently represent hydrogen or C<sub>1-6</sub> alkyl; and R<sub>c</sub> represents hydrogen, halogen, C<sub>1-6</sub> alkyl, CF<sub>3</sub>, OCF<sub>3</sub>, N(CH<sub>3</sub>)<sub>3</sub>, COC<sub>1-6</sub> alkyl, or methoxy;

## Table 2

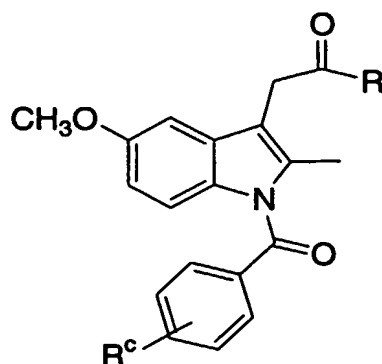


wherein R represents:

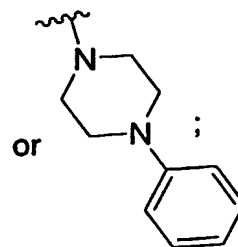
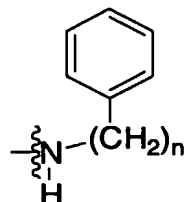
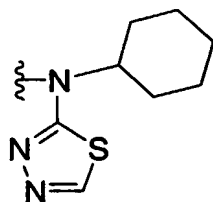
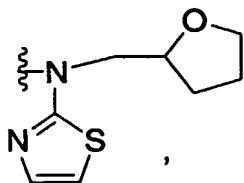
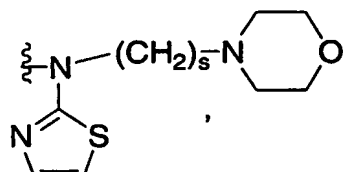
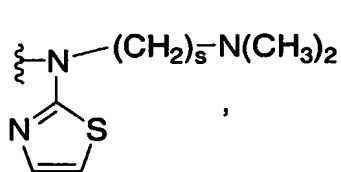
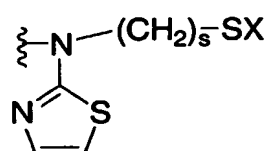
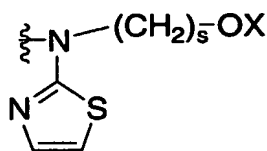
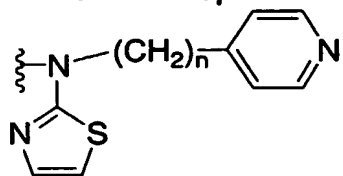


n is 0 to 3; s is 1-5; X represents hydrogen or C<sub>1-6</sub> alkyl; R<sup>b</sup> and R<sup>a</sup> independently represent hydrogen, methoxy, CO<sub>2</sub>X, NHAc, or C<sub>1-6</sub> alkyl; R<sup>c</sup> represents hydrogen, halogen, C<sub>1-6</sub> alkyl, CF<sub>3</sub>, OCF<sub>3</sub>, N(CH<sub>3</sub>)<sub>2</sub>, COC<sub>1-6</sub> alkyl, or methoxy

Table 3

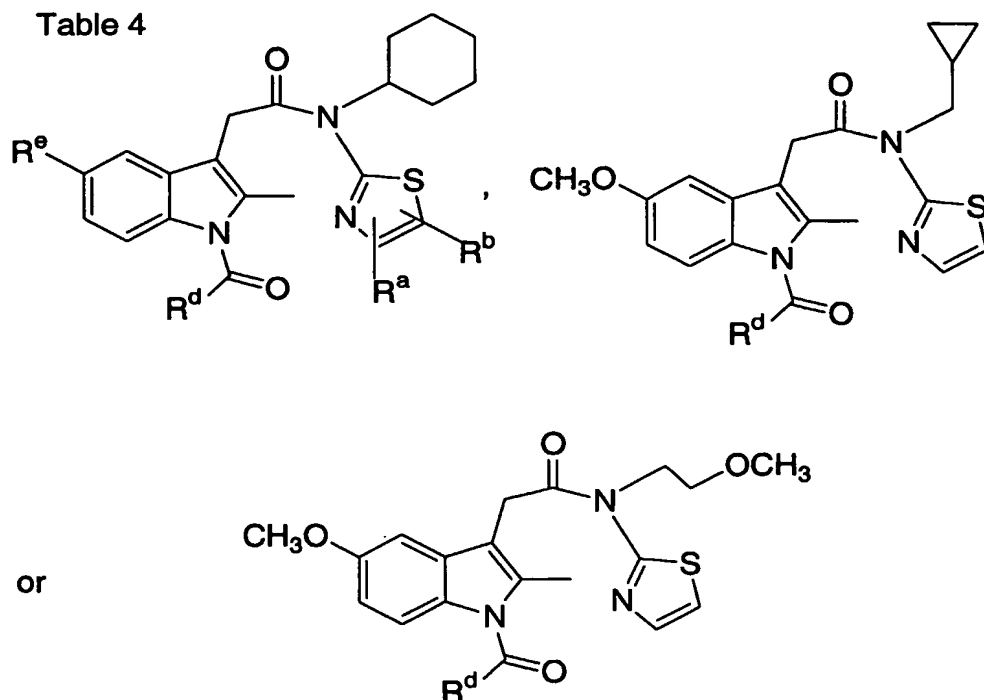


wherein R represents:



$n$  is 0 to 3;  $s$  is 1-5;  $X$  represents hydrogen or  $C_{1-6}$  alkyl; and  $R^c$  represents hydrogen, halogen,  $C_{1-6}$  alkyl,  $CF_3$ ,  $OCF_3$ ,  $N(CH_3)_2$ ,  $COC_{1-6}$  alkyl, or methoxy

Table 4



wherein:

$R^b$  and  $R^a$  independently represent hydrogen, methoxy,  $\text{CO}_2\text{X}$ ,  $\text{NHAc}$ , or  $\text{C}_{1-6}$  alkyl;

$R^d$  represents  $\text{C}_{1-6}$  alkyl, pyridinyl, -O-phenyl, phenyl, thienyl, said pyridinyl and phenyl optionally substituted with 1-3 halogen,  $\text{CF}_3$ ,  $\text{OCF}_3$ ,  $\text{N}(\text{CH}_3)_2$ , methoxy or  $\text{C}_{1-6}$  alkyl; and

$R^e$  represents methoxy,  $\text{O}(\text{CH}_2)_2\text{N}(\text{CH}_3)_2$ , or  $\text{OH}$ ;

or a pharmaceutically acceptable salt, enantiomer, diastereomer or mixture thereof.

- 5                    14.    The method according to claim 12 wherein the compound of the formula I is administered in a formulation selected from solution topical formulation and a suspension topical formulation.

15. A method according to claim 14 wherein an active ingredient belonging to the group consisting of:  $\beta$ -adrenergic blocking agent, parasympathomimetic agent, carbonic anhydrase inhibitor, and a prostaglandin or a prostaglandin derivative is optionally added to the formulation.

5

16. A method according to claim 21 wherein the  $\beta$ -adrenergic blocking agent is timolol; the parasympathomimetic agent is pilocarpine; the carbonic anhydrase inhibitor is dorzolamide, acetazolamide, metazolamide or brinzolamide; the prostaglandin is latanoprost or rescula, and the prostaglandin derivative is a hypotensive lipid derived from PGF2 $\alpha$  prostaglandins.

10

17. A method for treating macular edema or macular degeneration, increasing retinal and optic nerve head blood velocity or increasing retinal and optic nerve oxygen tension, or providing a neuroprotective effect comprising administration to a patient in need of such treatment a pharmaceutically effective amount of a compound of claim 1; or a pharmaceutically acceptable salt, enantiomer, diastereomer or mixture thereof.

15

18. The method according to Claim 17 wherein the compound of formula I is applied as a topical formulation.

20

19. A method according to claim 18 in which the topical formulation optionally contains xanthan gum or gellan gum.

25

20. A method of preventing repolarization or hyperpolarization of a mammalian cell wherein the cell contains a potassium channel comprising the administration to a mammal, including a human, in need thereof, of a pharmacologically effective amount of a compound according to claim 1, or a pharmaceutically acceptable salt, enantiomer, diastereomer or mixture thereof.

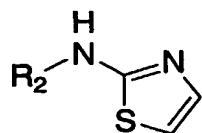
30

21. A method of treating Alzheimer's Disease, depression, cognitive disorders or arrhythmia disorders in a patient in need thereof comprising administering a pharmaceutically effective amount of a compound according to Claim 1, or a pharmaceutically acceptable salt, enantiomer, diastereomer or mixture thereof.



22. A method of treating diabetes in a patient in need thereof comprising administering a pharmaceutically effective amount of a compound according to claim 1, or a pharmaceutically acceptable salt, enantiomer, diastereomer or mixture thereof.

23. A process for making a compound of formula Ia:

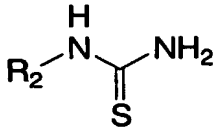


11

wherein R<sub>2</sub> is C<sub>1-10</sub> alkyl, C<sub>1-6</sub> alkylSR, -(CH<sub>2</sub>)<sub>n</sub>O(CH<sub>2</sub>)<sub>m</sub>OR,

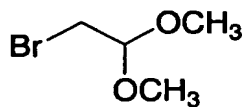
10 -(CH<sub>2</sub>)<sub>n</sub>C<sub>1-6</sub> alkoxy, -(CH<sub>2</sub>)<sub>n</sub>C<sub>3-8</sub> cycloalkyl, -(CH<sub>2</sub>)<sub>n</sub>C<sub>3-10</sub> heterocyclyl, -(CH<sub>2</sub>)<sub>n</sub>C<sub>5-10</sub> heteroaryl, -N(R)<sub>2</sub>, -COOR, or -(CH<sub>2</sub>)<sub>n</sub>C<sub>6-10</sub> aryl,

comprising adding to an alcohol suspension of compound 9:



9

15 a compound of formula 10:



10

and concentrated HCl and heating at reflux to give a compound of formula 11.

24. A process according to claim 23 wherein the alcohol is ethanol, methanol, isopropanol, butanol, pentanol or hexanol.